

I claim:

1. A subtelomeric probe useful for detecting chromosomal rearrangements comprising:

a single copy DNA sequence having a length of less than 25 kb, said sequence being capable of hybridizing to the terminal G-band or R-band of an arm of a single chromosome.

2. The probe of claim 1, said terminal band being light after G-band staining.

3. The probe of claim 1, said terminal band being dark after R-band staining.

4. The probe of claim 1, said arm of said single chromosome being selected from the group consisting of 1p, 1q, 2p, 2q, 3p, 3q, 4p, 4q, 5p, 5q, 6p, 6q, 7p, 7q, 8p, 8q, 9p, 9q, 10p, 10q, 11p, 11q, 12p, 12q, 13q, 14q, 15q, 16p, 16q, 17p, 17q, 18p, 18q, 19p, 19q, 20p, 20q, 21q, 22q, Xp, Xq, and Yp.

5. The probe of claim 1, said probe being selected from the group consisting of SEQ ID NOS. 1- 3, 5-23, 26-36, 38-57, 59-61, 63-67, 69-82, and 245-251.

6. The probe of claim 1, said probe having a length of less than 10 kb.

7. The probe of claim 1, said probe being within 8000 kb of the telomere of said chromosome.

8. The probe of claim 7, said probe being selected from the group consisting of SEQ ID NOS. 1- 3, 5-23, 26-36, 38-57, 59-61, 63-67, 69-82, and 245-251

9. The probe of claim 1, said probe being within 300 kb of the telomere of said chromosome.

10. The probe of claim 9, said probe being selected from the group consisting of SEQ ID NOS. 36, 80, 46, 47, 49, 51, 56, 248, 57, 78, 59, 75, 76, 74, 63, 250, 251, 66, 65, 67, 4, 3, 1, 9, 6, 11, 10, 17, 20, 19, 18, 21, 81, 26, 29, 28, 31, 32, 43, 42, 41, 40, 44, 45, and 70.

5 11. The probe of claim 1, said probe being labeled or being modified to attach to a surface.

12. A method of developing single copy DNA sequence probes from subtelomeric regions of chromosomes, said probes being able to hybridize to a single location  
10 in the genome, said method comprising the steps of:

searching the DNA sequence of said chromosome on a nucleotide-by-nucleotide basis  
beginning at the terminal nucleotide for a single copy interval of at least 500 base  
pairs in length that is closest to said terminal nucleotide;  
identifying said single copy interval;  
15 synthesizing said single copy interval; and  
using said synthesized single copy interval as said probes.

13. The method of claim 12, said identifying step including the step of  
verifying computationally or experimentally that said identified single copy interval is  
20 represented at a single genomic location or where paralogous sequences are closely linked so that  
only a single signal is detected.

14. The method of claim 13, said identifying step including verifying  
computationally and experimentally.

25 15. The method of claim 13, said computational verification including using  
software to determine that the probe sequence is located at a single position in the genome.

16. The method of claim 12, said method further including the step of labeling  
30 said synthesized single copy sequence.

17. The method of claim 13, said experimental verification including rehybridizing said single copy probe to said chromosome and visualizing said probe on the terminal band and correct arm of said chromosome.

5 18. The method of claim 12, said single copy interval being selected from the group consisting of SEQ ID NOS. 1- 3, 5-23, 26-36, 38-57, 59-61, 63-67, 69-82, and 245-251.

19. The method of claim 12, said method further comprising the step of preannealing said single copy probe with highly repetitive DNA.

10 20. A synthetic single copy polynucleotide for identifying chromosomal rearrangements, said polynucleotide being located within 8,000 kb of the terminal nucleotide of a chromosome and hybridizing to a single location on a specific chromosome when no chromosomal rearrangement has occurred, said polynucleotide having a length of less than 25  
15 kb.

21. The polynucleotide of claim 20, said polynucleotide being found in the terminal G-band or R-band of said specific chromosome.

20 22. The polynucleotide of claim 20, said polynucleotide being selected from the group consisting of SEQ ID NOS. 1- 3, 5-23, 26-36, 38-57, 59-61, 63-67, 69-82, and 245-251.

23. The polynucleotide of claim 20, said polynucleotide being located within  
25 about 300 kb of said terminal nucleotide of said specific chromosome.

24. The polynucleotide of claim 23, said polynucleotide being selected from the group consisting of SEQ ID NOS. 36, 80, 46, 47, 49, 51, 56, 248, 57, 78, 59, 75, 76, 74, 63, 250, 251, 66, 65, 67, 4, 3, 1, 9, 6, 11, 10, 17, 20, 19, 18, 21, 81, 26, 29, 28, 31, 32, 43, 42, 41, 40,  
30 44, 45, and 70.

25. The polynucleotide of claim 20, said polynucleotide being labeled or being chemically modified to attach to a surface.

26. An oligonucleotide primer pair used for deriving single copy probes that  
5 can detect chromosomal rearrangements, said primers comprising:  
a sequence selected from the group consisting of SEQ ID NOS. 83-244.

27. An improved synthetic DNA probe operable for detecting chromosomal rearrangements, said probe including a DNA sequence operable to hybridize to a precise location  
10 on a single chromosome arm wherein the improvement comprises a probe of less than 25 kb in length.

28. The improved probe of claim 27, said portion comprising the entire probe.

29. The improved probe of claim 27, said probe having at least a portion thereof being located closer to the end of a telomere on a chromosome arm than a clone selected from the group consisting of cosmids, fosmids, bacteriophage, P1, and PAC clones derived from half YACS, said chromosome arm being selected from the group consisting of 2p, 3p, 5p, 7p, 8p, 10p, 11p, 12p, 16p, 17p, 18p, Xp, Yp, 1q, 3q, 4q, 6q, 7q, 8q, 9q, 10q, 11q, 12q, 13q, 14q, 15q,  
20 16q, 17q, 18q, 19q, 20q, 21q, and 22q.

30. The improved probe of claim 27, said probe being located within 8,000 kb of the terminal nucleotide of the telomere of said chromosome.

31. The improved probe of claim 27, said probe being located within 300 kb of the terminal nucleotide of the telomere of said chromosome.

32. The improved probe of claim 27, said probe being located in the terminal G-band or R-band of said chromosome.

33. The improved probe of claim 27, said probe being selected from the group consisting of SEQ ID NOS. 46, 47, 49, 56, 78, 59, 64, 249, 2, 4, 3, 5, 9, 11, 20, 19, 21, 81, 246,

70, 72, 73, 36, 80, 247, 50, 57, 75, 76, 74, 63, 250, 66, 65, 67, 1, 6, 10, 12, 16, 15, 13, 14, 17, 18, 81, 245, 26, 31, 32, 43, 42, 41, 40, 44, and 45.

34. A method of screening an individual for cytogenetic abnormalities, said individual having either idiopathic mental retardation or mental retardation and at least one other clinical abnormality or cancer said method comprising the steps of:

screening the genome of the individual using a plurality of hybridization probes, each of said probes having a length of less than about 25 kb; and  
detecting hybridization patterns of said probes, said hybridization patterns indicating cytogenetic abnormalities in said genome.

35. The method of claim 34, said method further including the step of associating said hybridization patterns with specific clinical abnormalities.

36. The method of claim 34, said probes being represented at a single genomic location or where paralogous sequences are closely linked so that only a single hybridization signal is detected.

37. A method of delineating the extent of a chromosome imbalance comprising the steps of:

assaying a chromosome arm using at least one hybridization probe having a length of less than about 25 kb;  
detecting hybridization patterns of said probes on said arm; and  
comparing said hybridization patterns with a standard genome map of said arm in order to delineate the extent of a chromosome imbalance.

38. The method of claim 37, said method further including the step of correlating imbalances on said arm with a medical condition selected from the groups consisting of idiopathic mental retardation or cancer.

39. The method of claim 37, said method utilizing a plurality of probes.

40. The method of claim 37, said probe hybridizing to a specific chromosome arm.